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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,807	07/28/2003	Reiner L. Gentz	PF122P1D1C1	4342

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,807	GENTZ ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07282003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/595,927, which is a divisional of U.S. Application Serial Number 08/842,234, which is a continuation-in-part of U.S. Application Serial Number 08/264,003.

Claims 1-10 are currently pending and are the subject of examination in the present Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible asserted utility or a well-established utility.

The claims are most broadly drawn to antibodies directed to "a) a protein consisting of amino acid residues 1-147 of SEQ ID NO: 2, b) a protein consisting of amino acid residues 2-147 of SEQ ID NO: 2, c) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75771, and d) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75771, minus the N-terminal methionine."

The polypeptide of SEQ ID NO: 2 to which the claimed antibodies are directed is not supported by either a specific and substantial asserted utility or a well-established utility. SEQ ID NO: 2 is asserted on page 4 of the instant specification to be structurally related to the human FLAP (5-lipoxygenase activating protein) family. Paragraphs [0021] and [0022] of the instant specification disclose that the sequence of a nucleic acid sequence was determined from a "cDNA library derived from aorta endothelial cells induced with tumor necrosis factor α." The sequence of the putative polypeptide sequence of SEQ ID NO: 2 was then deduced from this sequence and determined to have 34% identity and 51% similarity over the entire coding sequence to human FLAP protein. The specification further discloses that residues 42-61 have "significant homology" (55%) to a "highly conserved region of FLAP I across many different species." The specification does not clearly indicate as to whether instant SEQ ID NO: 2 shares 55% homology with each of those "many different species" or whether the "significant homology" is only to the

human "FLAP I" protein of the prior art (Vickers et al. J. Lipid Mediat. [1993] 6:31-42; K on form PTO-1449).

A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Identifying a DNA segment derived from cDNA fragments and determining a relationship of a deduced putative polypeptide product to a database polypeptide sequence based solely on primary polypeptide sequence does not endow the polypeptide with well established utility. There is no clear guidance from the specification regarding the function of SEQ ID NO: 2 or that the polypeptide would have the same or similar biological properties as FLAP because the "homology" of the computer deduced protein of SEQ ID NO: 2 is based solely upon computer alignment with known sequences of the cDNA sequences from which the amino acid sequence was deduced. There would be no predictability that this homology would render the biological activities of the putative polypeptide of SEQ ID NO: 2 and FLAP similar because Applicant has not disclosed whether the biological activity of both polypeptides resides within the common region(s) or elsewhere within the sequence of the polypeptides, nor does the specification indicate whether the proteins share conserved active or binding sites. Whisstock et al (Quarterly Rev. Immunol. [2003] 36(3):307-340; U2 on form PTO-892) discloses that structure-based identification of homologues can be more reliable than sequence-alone-based methods of determining a protein's function but that "prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions" (Abstract, Figure 2 and Section 5 in particular). Whisstock further discloses inferring conservation patterns in members of a functionally uncharacterized family of proteins is tenuous and are just "reasonable guesses" (Abstract in particular). Brenner et al. (Proc. Natl. Acad. Sci. USA [1998] 95:6073-6078; V on form PTO-892), at page 6076, column 2, states that, "Fig. 2 shows one of the many pairs of proteins with very different structures that nonetheless have high levels of identity over considerable aligned regions. Despite the high identity, the raw and the statistical scores for such incorrect matches are typically not significant. The principal reasons percentage identity does so poorly seems to be that it ignores information about gaps and about the conservative or radical nature of residue substitutions. From the PDB90D-B analysis in Fig. 3, we learn that 30% identity is a reliable threshold for this database only for sequence alignments of at least 150 residues." Brenner therefore shows in Fig. 2 that reliance upon high identity alone in many pair wise comparisons is insufficient to relate information about structural and/or functional relatedness and in the analysis of Fig. 3 indicates that information which can be

gleaned from sequence identity comparisons is database-specific, not general. The Brenner reference puts further emphasis on the need for structural relationships on page 6074, end of first column in the statement, "Since the discovery that the structures of hemoglobin and myoglobin are very similar though their sequences are not, it has been apparent that comparing structures is a more powerful (if less convenient) way to recognize distant evolutionary relationships than comparing sequences." Therefore, the Brenner reference teaches that sequence identity alone is insufficient to establish functional relationships between proteins, rather it must be used in concert with structural information to accurately establish relationships between proteins. The instant specification does not provide any information on the structural characteristics of SEQ ID NO: 2, only an assertion of homology with FLAP, but this "homology" is based solely on the finding of sequence homology to FLAP, and not actual structural determination. According to Brenner, sequence homology must be used in concert with structural information, rather than using one to guess the other. The instant specification does not provide any information about the structure of the predicted SEQ ID NO: 2 polypeptide, only sequence homology to the prior art sequence human FLAP, and for this reason the specification provides insufficient information to enable the artisan to reasonably predict that SEQ ID NO: 2 is functionally related to FLAP and therefore the specification does not teach the artisan a credible utility for SEQ ID NO: 2.

Additionally, the specification does not assert any credible utility of the polypeptide of SEQ ID NO: 2. Because the characteristics of SEQ ID NO: 2 are based solely upon sequence identity of the protein with other previously known proteins and not based upon analysis of any actually-produced protein product, no biological activity has been established for SEQ ID NO: 2. As such, further research would be required to identify or reasonably confirm a "real world" context of use, for example, to identify any function of SEQ ID NO: 2 and conditions for which SEQ ID NO: 2 polypeptides would be of diagnostic or therapeutic significance. Accordingly, without a "real-world" use for the protein, antibodies specific therefore are equally not useful, as basic research such as studying the properties of the product of the polypeptide are not considered substantial and credible utility for the claimed invention. The only other utility asserted in the specification is as an inhibitor of the interaction of SEQ ID NO: 2 with 5-lipoxygenase in paragraphs [0071]-[0072]. However such a utility is not a credible specific or substantial utility because the binding of SEQ ID NO: 2 to 5-LO has not been established and it is not clear, therefore, whether there is even any interaction between SEQ ID NO: 2 and 5-LO for an antibody to inhibit, because said interaction is putative in nature, being based merely upon sequence comparisons and not any actual trials.

Therefore, the specification does not fairly disclose a substantial and credible utility for the antibody of the instant claims. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Information Disclosure Statement

3. Reference "C" on Applicant's form PTO-1449 has been initialed as considered but has been lined through because it represents a non-published application that is not claimed as a priority application in the instant application. Therefore, the application number should not appear on the face of a patent that may issue from the instant application.

Conclusion

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
December 1, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
12/13/04